

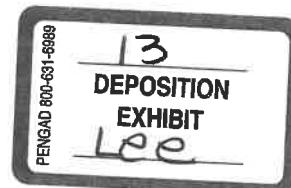
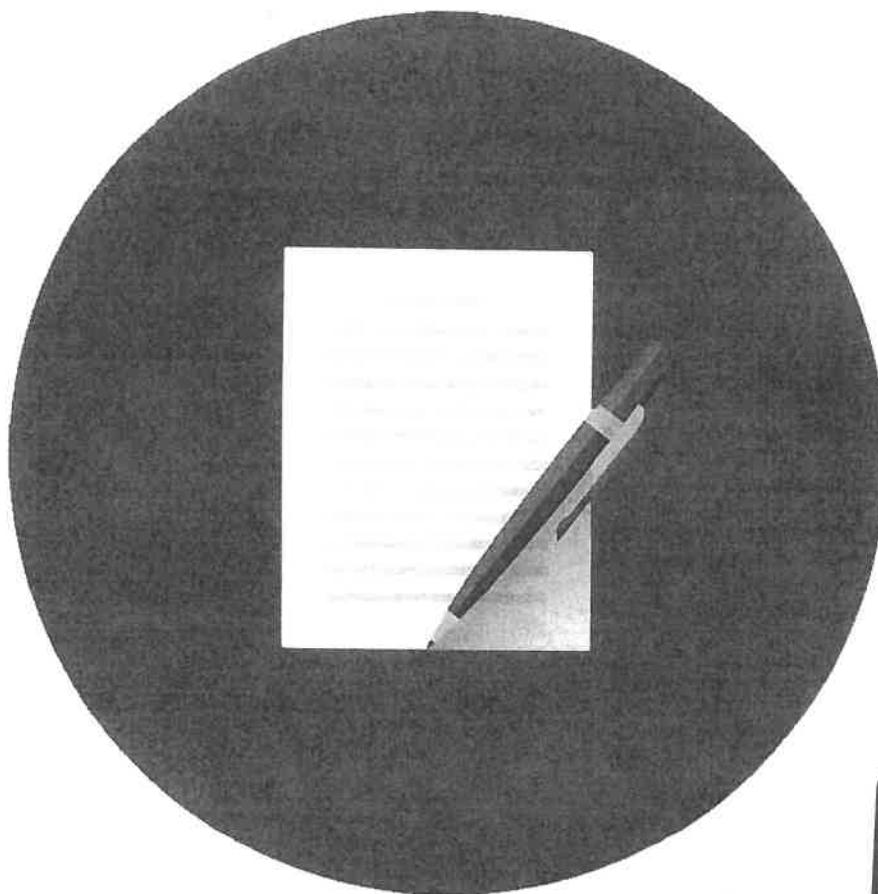
EXHIBIT T



Pregnancy

CDC Articles and Key Findings About Opioid Use During Pregnancy

Below are selected key findings and articles of interest published by CDC authors.



Key Findings

Identifying Babies Born Exposed to Opioids and Gabapentin Can Improve Treatment

A study by Marshall University, in collaboration with CDC, found that identifying babies exposed to opioids and gabapentin in the womb may result in better treatment and shorter hospital stays. Opioids and gabapentin are medicines used to treat some types of pain or to treat opioid use disorder. Healthcare providers should closely watch pregnant women with opioid use to carefully manage the medical care for both mother and baby during pregnancy and after delivery. One of the concerns is withdrawal symptoms in the newborn.

Read the full scientific article [↗](#) or summary key findings.

Gastroschisis Trends and Ecological Link to Opioid Prescription Rates in the United States, 2006–2015

Gastroschisis is a birth defect of the abdominal (belly) wall. Several studies show increased rates of babies born with gastroschisis over time. Most of these babies are born to young mothers. A study from the Centers for Disease Control and Prevention (CDC) found that the number of babies born with gastroschisis was higher in U.S. counties with high opioid (pain medicine) prescription rates, compared to those with low opioid prescription rates.

Key Findings:

- Researchers estimated that, from 2006-2015, about 1 in every 2,300 babies was born with gastroschisis in twenty U.S. states.
- This study looked at reported cases of gastroschisis by county in these states and found that counties where doctors frequently prescribe opioids had 1.6 times more babies born with gastroschisis compared to counties with low opioid prescription rates.
- Researchers aren't currently able to explain why gastroschisis rates are more common in these counties. More research is needed to understand what factors may contribute to this observed association.

Tracking rates of birth defects and opioid prescriptions are key to understanding how mothers and babies may be impacted by the opioid crisis.

Read the full scientific article.

Public Health Reporting of NAS Offers Opportunities for Treatment and Prevention

A CDC article looked at laws enacted in six states that make health departments or hospitals report all babies born with neonatal abstinence syndrome (NAS) for public health monitoring.

Key Findings:

- State officials noted that required reporting of infants born with NAS has helped their state
 - Estimate the number of babies born with NAS in real time.
 - Locate specific areas more severely impacted by NAS to help target resources.
 - Identify mothers and babies affected by opioid use disorder who may benefit from local programs and services.
- States that require hospitals to report NAS cases may need additional resources and training for healthcare providers and hospital staff. This can help ensure that high-quality information is collected.
- This report found that states use different criteria and approaches for public health reporting of NAS. States considering implementation of laws requiring NAS case reporting for public health surveillance can benefit from understanding advantages and challenges of the approaches used.

Read the full scientific article.

Opioids Prescribed Just Before Pregnancy Associated With Autism

A study from the Waisman Center at the University of Wisconsin-Madison, in collaboration with CDC, found that mothers who were prescribed opioids just before becoming pregnant were more likely to have a child with autism spectrum disorder (ASD) or a child with other developmental disabilities (DDs) and some autism symptoms.

Key Findings:

- Mothers who were prescribed opioids just before becoming pregnant (1.2% of mothers with a child in the ASD group) were about 2.5 times more likely to have a child with ASD or a child with other DDs and some autism symptoms.
- In this sample, about 8% of mothers reported receiving an opioid prescription just before or during pregnancy. The majority (76%) of these mothers received only one prescription. The most common reasons for opioid prescriptions were migraine headaches, injury, and back pain. Illicit opioid use was not included in this analysis.

This study is among the first to assess associations between prescription of opioids in pregnancy and ASD and other DDs. Researchers were limited by small sample sizes and were not able to assess whether the associations found were related to the opioid medication itself, to the reason the mother took the medication, or to some other unknown factor associated with the opioid use. More research is needed to better understand developmental outcomes among children whose mothers used opioids during pregnancy.

Read the scientific summary [\[2\]](#).

Opioid Use Disorder Documented at Delivery Hospitalization — United States, 1999–2014

The number of pregnant women with opioid use disorder (OUD) at labor and delivery more than quadrupled from 1999 to 2014, according to an analysis by CDC. This first-ever, multi-state analysis of trends, published in CDC's *Morbidity and Mortality Weekly Report*, reveals significant increases in the 28 states with available data.

Key Findings:

- The national prevalence rate of OUD among pregnant women increased from 1.5 per 1,000 delivery hospitalizations in 1999 to 6.5 in 2014. On average, the national prevalence rate grew by 0.39 cases per 1,000 each year.
- From 1999–2014, the average annual rate increases were lowest in California and Hawaii (growth of less than 0.1 cases per 1,000 each year) and highest in Maine, New Mexico, Vermont, and West Virginia (all with an increase of more than 2.5 cases per 1,000 each year).

Read the full scientific article.

Educational Disabilities among Children Born with Neonatal Abstinence Syndrome

In this study, published in *Pediatrics*, the Tennessee Department of Health, supported by CDC and March of Dimes, looked at longer-term educational outcomes among children born with NAS in the United States by linking Tennessee Medicaid data with birth certificate and state educational data. Researchers found that children born with NAS were more likely than children without NAS to be evaluated for an educational disability, to be diagnosed with a developmental delay or speech/language impairment, and to have received classroom support or speech therapy.

Read the scientific abstract [\[2\]](#) or summary key findings.

Maternal Use of Opioids during Pregnancy and Congenital Malformations: A Systemic Review

In this report, published in *Pediatrics*, CDC researchers reviewed previous studies to better understand what is currently known about opioids use during pregnancy and birth defects.

Specifically, the review [\[2\]](#) found:

- Use of opioids during pregnancy may be linked to various birth defects such as oral clefts, congenital heart defects, and clubfoot [\[2\]](#).
- However, many of the studies reviewed had issues with study methods and quality.

More research is needed to understand the connections between individual types of opioids and specific birth defects. Until more is known, women of childbearing age considering opioid treatment should discuss the risks and benefits with their healthcare providers.

Read the scientific abstract [\[2\]](#).

Incidence of Neonatal Abstinence Syndrome — 28 States, 1999–2013

In this *Morbidity and Mortality Weekly Report*, CDC analyzed neonatal abstinence syndrome (NAS) trends in 28 states using hospital discharge data from 1999 through 2013, and found the rate of NAS had increased 300%.

Key Findings:

- From 1999 through 2013, the rate of NAS increased from 1.5 per 1,000 hospital births in 1999 to 6.0 cases per 1,000 hospital births. In 2013, more than 8,000 newborns were born with NAS, compared to about 2,000 newborns in 1999.
- In 2013, there was considerable variation in NAS incidence rates by state, ranging from 0.7 (Hawaii) to 33.4 (West Virginia) cases per 1,000 hospital births.

Read the full scientific article.

CDC Grand Rounds: Public Health Strategies to Prevent Neonatal Abstinence Syndrome

In this *Morbidity and Mortality Weekly Report*, CDC reports on public health strategies to prevent NAS outlined in a recent Public Health Grand Rounds presentation.

These include:

- Ensuring appropriate opioid prescribing that's in line with the "CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016."
- Maximizing and enhancing prescription drug monitoring programs (PDMPs) [PDF – 7.89 MB], state-based databases that collect, monitor, and analyze controlled substance dispensing.
- Increased access to preconception health care and quality family planning services.

Read the full scientific article.

Opioid Prescription Claims among Women of Reproductive Age — United States, 2008–2012

In 2015, CDC's *Morbidity and Mortality Weekly Report* published a study looking at how often women aged 15–44 years filled a prescription for opioid pain medications.

Key Findings:

- During 2008–2012, more than one-quarter of privately insured and over one-third of Medicaid-enrolled women aged 15–44 years filled a prescription written by a healthcare provider for an opioid medication.
- The most commonly prescribed opioids were hydrocodone, codeine, and oxycodone.

Read the full scientific article or summary key findings.

CDC Articles of Interest

National Trends in Hepatitis C Infection by Opioid Use Disorder Status Among Pregnant Women at Delivery Hospitalization — United States, 2000–2015
Ko JY, Haight SC, Schillie SF, Bohm MK, Dietz PM. *MMWR Morb Mortal Wkly Rep*. 2019;68:833–838.

State Strategies to Address Opioid Use Disorder Among Pregnant and Postpartum Women and Infants Prenatally Exposed to Substances, Including Infants with Neonatal Abstinence Syndrome.
Kroelinger CD, Rice ME, Cox S, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68:777–783.

Obstetrician–Gynecologists' Practice Patterns Related to Opioid Use During Pregnancy and Postpartum—United States, 2017
Ko JY, Tong VT, Haight SC, et al. *J Perinatol*. 2019

Treatment of Substance Use Disorders among Women of Reproductive Age by Depression and Anxiety Disorder Status, 2008-2014 (*Journal of Women's Health*, August 2019). Zhou J, Ko JY, Haight SC, Tong VT, et al. *J Womens Health*.

Standardization of State Definitions for Neonatal Abstinence Syndrome Surveillance and the Opioid Crisis (*American Journal of Public Health*, August 2019) Chiang KV, Okoroh EM, Kasehagen LJ, Garcia-Saavedra LF, Ko JY. *Am J Public Health*. 2019;109(9):1193-1197.

Leveraging existing birth defects surveillance infrastructure to build neonatal abstinence syndrome surveillance systems — Illinois, New Mexico, and Vermont, 2015–2016 Lind JN, Ailes EC, Alter CC, Fornoff JE, Brozicevic P, Garcia Saavedra LF, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68(7):177—80.

Public Health Surveillance of Prenatal Opioid Exposure in Mothers and Infants Honein MA, Boyle C, Redfield RR. *Pediatrics*. 2019;143(3):e20183801.

Gastroschisis Trends and Ecological Link to Opioid Prescription Rates in the United States, 2006-2015 Short TD, Stallings EB, Isenburg J, O'Leary LA, Yazdy MM, Bohm M, et al. *MMWR Morb Mortal Wkly Rep*. 2019; 68: 31-36.

Evaluation of State-Mandated Reporting of Neonatal Abstinence Syndrome — Six States, 2013–2017 Jilani SM, Frey MT, Pepin D, Jewell T, Jordan M, Miller AM, et al. *MMWR Morb Mortal Wkly Rep*. 2019; 68(1):6-10.

Brief Report: Maternal Opioid Prescription from Preconception Through Pregnancy and the Odds of Autism Spectrum Disorder and Autism Features in Children. Rubenstein E, Young JC, Croen LA, DiGuiseppi C, Dowling NF, Lee LC, et al. *J Autism Dev Disord*. 2019;49(1):376-82.

Opioid use disorder documented at delivery hospitalization – United States, 1999—2014 Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. *MMWR Morb Mortal Wkly Rep*. 2018;67(31):845—49.

Maternal use of opioids during pregnancy and congenital malformations: A systematic review Lind JN, Interrante JD, Ailes EC, Gilboa Sm, Khan S, Frey MT, et al. *Pediatrics*. 2017;139(6):e20164131.

Incidence of neonatal abstinence syndrome – 28 states, 1999—2013 Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. *MMWR Morb Mortal Wkly Rep*. 2016;65(31):799—802.

Opioid prescription claims among women of reproductive age—United States, 2008—2012 Ailes EC, Dawson AL, Lind JN, Gilboa SM, Frey MT, Broussard CS, et al. *MMWR Morb Mortal Wkly Rep*. 2015;64(2):37—41.

Periconceptional use of opioids and the risk of neural tube defects Yazdy MM, Mitchell AA, Tinker SC, Parker SE, Werler MM. *Obstet Gynecol*. 2013;122:838—44.

Maternal treatment with opioid analgesics and risk for birth defects Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso, et al. *Am J Obstet Gynecol*. 2011;204:314.e1–314.e1—11.